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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/601,497	06/23/2003	Ching-Yu Lin	4712-117.1 US	4733

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EXAMINER	
POHNERT, STEVEN C	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 10/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/601,497	LIN ET AL.	
	Examiner	Art Unit	
	Steven C. Pohnert	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-23* is/are pending in the application.

4a) Of the above claim(s) *23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-22* is/are rejected.

7)☐ Claim(s) *16-22* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 June 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/11/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group 1 a detector drawn a combination of all HPVs recited (claims 16-23 which correspond to claims 1-7 and 15 of initial claims) in the reply filed on February 21, 2006 is acknowledged. The traversal is on the ground(s) that "Search of the detectors of Group I would uncover the method of group II." This is not found persuasive because as stated in the restriction requirement the detectors of group I can be used for a materially different process, such as mutational analysis. As the product claimed can be used in a materially different process, the groups are distinct (MPEP § 806.5(h)).

Claim 23 is withdrawn from consideration as being non-elected. In response to the restriction applicant elected, "The combination of all recited subtypes of claim 1." As claim 23 is drawn to a single probe, it does not encompass all the subtypes recited in claim 1, instant claim 16.

The requirement is still deemed proper and is therefore made FINAL.

An office action on the merits of claims 16-22 follows.

Claim Objections

2. Claims 16-22 are objected to because of the following informalities:

Claims17-22 refer to claim 1. Examiner notes this may be a typographical error due to the cancellation of claims, as claim 1 has been canceled.

Claims 17-22 are being read drawn to the detector of claim 16.

Claim 16 is objected to as it recites "said HPV subtype is one selected from...." In response to the restriction requirement applicant elected, "The combination of all recited subtypes of claim 1." Claim 16 thus requires amendment so it corresponds to election.

Claims 16 and 17 are drawn to HPV CP8034. Examiner notes this may be a typographical error, as the specification states, "The sequences of the fragments of each subtype described in the invention are publicly available...." (see page 13, paragraph 46). The specification teaches both CP8034 and CP8304, however only CP8304 was found in the art.

The MPEP §2105 states, "An amendment to correct an obvious error does not constitute new matter where one skilled in the art would not only recognize the existence of the error in the specification, but also recognize the appropriate correction."

Appropriate correction is required.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 17-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 17-22 are drawn to the detector of claim 1, however claim 1 has been canceled. As claim 1 has been canceled, the skilled artisan would be unable to

determine the metes and bounds of claims 17-22. In the interest of furthering prosecution the examiner has interpreted the claims as if they depend from claim 16.

Claim 22 is dawn to the use of glutaldehyde-3-phosphodehydrogase (GAPDH) microdots as an internal control. One of skill in the art would not be able to determine if the claim was drawn to glutaldehyde-3-phosphodehydrogase or GAPDH. A review of the art did not result in references to glutaldehyde-3-phosphodehydrogase. GAPDH in the art refers to glyceraldehyde-3-phosphate dehydrogenase. GAPDH is a very well known and common control. SEQ ID NO 471 and 472 of the specification are directed to GAPDH. In the interest of furthering prosecution, claim 22 has been interpreted as directed to GAPDH or glyceraldehyde-3-phosphate dehydrogenase, for art purposes.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 16, 17, 18, 20, and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bauer et al (US Patent 5527898) in view of 1997 HPV compendium, accession number AB027021 GI: 6970427 and Chow et al (Journal of General Virology, 1999, volume 80, pages 2923-2929) and Kino et al (Clinical and Diagnostic laboratory Immunology, 2000, volume 7, pages 91-95) and Hogan et al (US Patent 5541308).

The term "microdots" is not defined in the specification. The claims have been given the broadest reasonable interpretation of microdots as oligonucleotide probes bound to a membrane.

The term "biochip" is not defined in the specification. The claims have been given the broadest reasonable interpretation as drawn to a membrane with oligonucleotide probes fixed to a solid support.

Bauer teaches human papilloma virus (HPV) has been linked to cancer (see column 1, lines 30-32). Bauer teaches different types of HPV have present different risks to affected individuals (see column 1, lines 42-23). Bauer et al teaches a reverse dot blot system to detect HPV (see column 54, example 5). Bauer teaches the membrane bound oligonucleotide probes are fixed in discrete location (see column 54 line 51-52). Bauer teaches probes to the L1 region of HPV (see Table 5 and 5a). Bauer teaches the L1 sequence of HPVs 26, 31, 35, 39, 40, 42, 45, 51, 52, 53, 54, 55, 56, 57, and 59 (see SEQ ID NOs 14-20, 273-296). Bauer teaches hybridizing type specific probes to HPV 26, 31, 35, 39, 40, 42, 45, 51, 52, 53, 54, 55, 56, 57, and 59 for determining HPV type by hybridization (see column 3 lines 9-16) following amplification with MY11 and MY09 primers. Bauer teaches the type specific probes are 18-20 nucleotides (claim 21) in length with a T_m of 58°C to 64°C (see column 9 lines 15-19). Bauer further teaches the diversity of HPV demonstrates the need for type specific probes (see column 18, lines 45-51). Bauer teaches type specific probes attached to a nylon membrane (claims 18 and 20) (see column 55, line 6). Bauer teaches this approach has led to the discovery of previously unknown or uncharacterized HPV types

(see column 7, lines46-48). Bauer teaches the identification of new HPV's by his method, require new probes for detection and typing (see column 7, 52-55). Bauer thus teaches the use of a carrier comprising a plurality of microdots to detect and type HPV.

Bauer does not teach detection probes to HPV 6, HPV 11,HPV 16, HPV 18, HPV 32, HPV 33, HPV 37, HPV 43, HPV 44, HPV 58, HPV 61, HPV 62, HPV 66, HPV 67, HPV 68, HPV 69, HPV 70, HPV 72, HPV 74, HPV 82, HPV CP8061, HPV CP8034, HPV L1AE5, HPV MM4, HPV MM7 and HPV MM8.

However, the 1997 HPV compendium teaches the L1 sequence of all recited HPVs (see page I5-I7), except HPV82 and HPVL1AE5, which are taught by accession number AB027021 GI: 6970427 and Chow et al. The 1997 HPV compendium further teaches the alignment of L1 nucleotide sequences it teaches (see II-L1-23-II-L1-73).

Chow teaches the sequence of HTL7474-S in figure 1b, which is the full length of HPV L1AE5 (see page 2924, second column, lines 8-10). Chow further teaches the screening of DNA from cervical specimens (see page 2923, 2nd column, lines 15-16). Chow further teaches the similarity of HTL7474-S to other highly oncogenic HPV types.

Kino et al teaches the molecular cloning and sequencing of HPV82 (see abstract). Kino et al use of an HPV82 DNA probe (see page 92, 2nd column, lines 6-7). Kino et al teaches any HPV detected by in situ hybridization in invasive cervical carcinoma should be considered high-risk HPV types (see page 91, 1st column, 22-23). Kino et al teaches detection of HPV 82 by in situ hybridization (see figure 1 D). Thus Kino teaches HPV82 is a high risk HPV subtype.

Hogan et al teaches probe design for detection of specific sequences (see abstract). Hogan teaches identification of variable regions (see column 6, lines 3-55). Hogan teaches that the target sequences should be aligned in the variable regions (see column 6 line 67—column 7, line 8) to identify probe regions. Hogan further teaches probes should be positioned to minimize stability of probe: nontarget hybrids, by avoiding GC rich regions of homology to non-target organisms and areas of mismatch (see column 7 lines 10-15). Hogan further teaches maximizing stability of the probe target hybrid, by avoiding long AT sequences and terminating hybrids with G: C base pairing and by designing probes with the appropriate T_m (see column 7 lines 16-19). Hogan teaches probes designed from these methods allow organisms to be distinguished from phylogenetic neighbors (column 2 lines 38-39) with accuracy, simplicity, economy and speed (column 3, lines 4-6)

Therefore it would be prima facie obvious to one of ordinary skill in the art at the time the invention was made to the improve Bauer's method of HPV detection and typing to include HPV 6, HPV 11, HPV 16, HPV 18, HPV 32, HPV 33, HPV 37, HPV 43, HPV 44, HPV 58, HPV 61, HPV 62, HPV 66, HPV 67, HPV 68, HPV 69, HPV 70, HPV 72, HPV 74, HPV 82, HPV CP8061, HPV CP8034, HPV L1AE5, HPV MM4, HPV MM7 and HPV MM8 taught in the 1997 HPV compendium and accession number AB027021 GI: 6970427 and Chow et al (Journal of General Virology, 1999, volume 80, pages 2923-2929). The ordinary artisan would be motivated to improve Bauer's method, because Bauer teaches HPV has been linked with cancer and the risk associated with each subtype is different. The ordinary artisan would further be motivated to include the

HPV types taught by the 1997 HPV compendium, accession numbers, and Chow, because Bauer teaches the need to make probes and distinguish HPV types. Further, Chow and Kino both teach on the oncogenic potential of different HPV subtypes and the use of probes for their HPV of interest. The ordinary artisan would be motivated to align the L1 region of HPV types and make probes for HPV 6, HPV 11, HPV 16, HPV 18, HPV 26, HPV 31, HPV 32, HPV 33, HPV 35, HPV 37, HPV 39, HPV 42, HPV 43, HPV 44, HPV 45, HPV 51, HPV 52, HPV 53, HPV 54, HPV 55, HPV 56, HPV 58, HPV 59, HPV 61, HPV 62, HPV 66, HPV 67, HPV 68, HPV 69, HPV 70, HPV 72, HPV 74, HPV 82, HPV CP8061, HPV CP8034, HPV L1AE5, HPV MM4, HPV MM7 and HPV MM8, because Hogan teaches alignment allows probe design maximize homology to target sequences and minimize homology to non-target sequences (see column 7 lines 3-8). The ordinary artisan would be motivated to align the L1 sequences of recited HPV types because Hogan teaches alignment allows probe design maximize homology to target sequences and minimize homology to non-target sequences. The ordinary artisan would further be motivated to align this region because Hogan teaches alignment of variable regions of DNA is a step in probe design. The ordinary artisan would be motivated by the teachings Bauer, the 1997 HPV compendium, AB027021 GI: 6970427, and Chow et al and Hogan to make probes specific to the HPV recited including probes with SEQ ID NO listed in claim 17. IT is noted that, Blast searches done with the probes in claim 17possessed 100% identity with the sequences taught by the 1997 HPV compendium, Bauer, Chow, and accession number cited.

Designing probes, which are equivalents to those taught in the art is routine experimentation. The prior art teaches the parameters and objectives involved in the selection of oligonucleotides that function as probes, see Hogan. Moreover there are many internet web sites that provide free downloadable software to aid in the selection of probes drawn from genetic data recorded in a spreadsheet. The prior art is replete with guidance and information necessary to permit the ordinary artisan in the field of nucleic acid detection to design probes. As discussed above, the ordinary artisan would be motivated to have designed and tested new probes to obtain additional oligonucleotides that function to detect specific HPV subtypes and identify oligonucleotides with improved properties. The ordinary artisan would have a reasonable expectation of success of obtaining additional probes from within the alignment provided by the 1997 HPV compendium, Chow et al, and sequence of accession numbers AB027021 GI: 6970427. Thus, for the reasons provided above, the ordinary artisan would have designed additional probes using the teachings in the art at the time the invention was made. The claimed SEQ ID NOs are obvious over the cited prior art, absent secondary considerations.

7. Claims 19 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bauer et al (US Patent 5527898), 1997 HPV compendium, Chow et al, accession number AB027021 GI: 6970427 and Hogan et al (US Patent 5541308) as applied to claims above 16-18, 20, and 21, and further in view of Lockhart et al (US Patent 6040138).

The teachings of Bauer et al (US Patent 5527898), 1997 HPV compendium, Chow et al, accession number AB027021 GI: 6970427 and Hogan et al (US Patent 5541308) are set forth above. Bauer et al, 1997 HPV compendium, Chow et al, accession number, AB027021 GI: 6970427 and Hogan et al do not teach the use of GAPDH as a control or glass as a carrier.

However, Lockhart et al teaches the use of glass as a support for an array of oligonucleotides (see column 19, lines 48-50) because glass allows direct synthesis of oligonucleotides on the solid support. Lockhart further teaches the use of GAPDH as constitutively expressed gene for normalization controls (see column 16, lines2-5 and 55-60).

Therefore it would have been prima facie obvious to one of skill in the art at the time the invention was made to improve HPV detection method of Bauer et, 1997 HPV compendium, Chow et al, accession number AB027021 GI: 6970427 and Hogan et al by using the glass support and GAPDH controls of Lockhart, because Lockhart teaches the glass support allows probe synthesis on the array and GAPDH probes allow normalization of data. The ordinary artisan would be motivated to use the glass support of Lockhart, because Lockhart teaches it allows oligonucleotide synthesis on the support. The ordinary artisan would be motivated to use GAPDH as a control, because Lockhart teaches GAPDH allows normalization of controls.

Conclusions

No claims are allowed over the cited prior art.

Summary

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Steven C. Pohnert whose telephone number is 571-272-3803. The examiner can normally be reached on Monday-Friday 7:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Steven Pohnert

JEHANNE SITTON
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9/26/06